Food Advisory Committee: Questions - Revised

I. Background

Under the authority of the Federal Food, Drug, and Cosmetic Act, FDA authorizes health claims in the labeling of conventional foods and dietary supplements. Claims must be reviewed by FDA before they may appear in labeling. In the FDA context, "health claim" does not have its usual broad meaning of any claim about health; rather, for FDA purposes, "health claim" means an express or implied labeling claim about the relationship between a food substance and a disease or health-related condition. FDA has defined "disease" by regulation as damage to an organ, part, structure, or system of the body such that it does not function properly, except for nutrient deficiency diseases. The agency has interpreted "health-related condition" to mean a state of health leading to disease.

For purposes of evaluating proposed health claims involving a disease (e.g., osteoarthritis), FDA has consistently identified two endpoints with which to identify disease risk reduction: a) reduction in incidence of the disease, and; b) beneficial changes in modifiable risk factors/surrogate endpoints for the disease.

FDA also refers to modifiable risk factors/surrogate endpoints for disease as "biomarkers" and defines them as:

> "a measurement of a variable related to a disease that may serve as an indicator or predictor of that disease. Biomarkers are parameters from which the presence or risk of a disease can be inferred, rather than being a measure of the disease itself. In conducting a health claim review, FDA does not rely on a change in a biomarker as a measurement of the effect of a dietary factor on a disease unless there is evidence that altering the parameter can affect the risk of developing that disease or health-related condition. This is the case for serum cholesterol in that high levels are generally accepted as a predictor of risk for coronary heart disease, and there is evidence that decreasing high serum cholesterol can decrease that risk. Therefore, the evaluation of whether decreasing the intake of dietary fat reduces the risk of developing heart disease took into account many studies that assessed changes in serum cholesterol, specifically LDL-cholesterol, rather than the development of heart disease per se. For the existing authorized health claims, acceptable biomarkers are LDL-cholesterol levels for coronary heart disease, measures of bone mass for osteoporosis, and measures of blood pressure for hypertension."[1]

FDA relies primarily on human studies that are primary reports of data collection when attempting to establish a diet-disease relationship.

[1] Guidance for Industry: Significant Scientific Agreement in the Review of Health Claims for Conventional Foods and Dietary Supplements, December 22, 1999 (http://www.cfsan.fda.gov/~dms/ssaguide.html).

II. Questions

1) a. Is joint degeneration a state of health leading to disease, i.e., a modifiable risk factor/surrogate endpoint (as discussed above) for OA risk reduction? What are the strengths and limitations of the scientific evidence on this issue ?

b. Is cartilage deterioration a state of health leading to disease, i.e., a modifiable risk factor/surrogate endpoint (as discussed above) for OA risk reduction? What are the strengths and limitations of the scientific evidence on this issue ?

2) a. If we assume that joint degeneration is a modifiable risk factor/surrogate endpoint for OA risk reduction and we assume that research demonstrates that a dietary substance treats, mitigates or slows joint degeneration in patients diagnosed with OA, is it scientifically valid to use such research to suggest a reduced risk of OA in the general healthy population (i.e., individuals without OA) from consumption of the dietary substance ?

b. If we assume that cartilage deterioration is a modifiable risk factor/surrogate endpoint for OA risk reduction and we assume that research demonstrates that a dietary substance treats, mitigates or slows cartilage deterioration in patients diagnosed with OA, is it scientifically valid to use such research to suggest a reduced risk of OA in the general healthy population (i.e., individuals without OA) from consumption of the dietary substance ?

3) If human data are absent, can the results from animal and in vitro models of OA be used to demonstrate risk reduction of OA in humans?

a. To the extent that animal or in vitro models of OA may be useful, what animal models, types of evidence, and endpoints should be used to assess risk reduction of OA in humans?

b. If limited human data are available, what data should be based on human studies and what data could be based on animal and in vitro studies to determine whether the overall data are useful in assessing a reduced risk of OA in humans?